VI. THE STATUS OF VACCINE DEVELOPMENT -- 1993

Although the principle of preventing infectious diseases through the use of vaccines was established experimentally in the 18dI century, most of the vaccines currently in use have been created since the 1930's (see figure 4). Today, over 20 major human diseases caused by bacteria or viruses can be prevented by the use of vaccines. In the United States, vaccines for such diseases as diphtheria, tetanus, pertussis (whooping cough), measles, mumps, rubella (German measles), and poliomyelitis have been available and widely used in children for many years. Recently, new vaccines, such as those for hepatitis B virus and *Haemophilus infiuenzae* type b (Hib), have been developed, licensed, and recommended for universal use in children.

In addition, other licensed vaccines, such as those for influenza and pneumococcal pneumonia, are used in populations at special risk (some of which, such as the elderly, are numerically quite large). Licensed vaccines for other special uses, such as the military or travelers, include those for adenovirus, plague, rabies, yellow fever, salmonella, and Japanese encephalitis. (See appendix 5 for a list of vaccines licensed in the United States).

NEW METHODS AVAILABLE FOR MAKING VACCINES

Translation of basic biomedical research into a licensed product has historically been a slow, sometimes uncertain, and costly process. Currently, it takes more than a decade to develop a successful vaccine (Institute of Medicine, 1993.b). As with drug development, few of the candidates that enter the early stages of animal or clinical testing emerge as effective vaccines suitable for licensure.

The biotechnology revolution has significantly expanded our capability to develop vaccines. Since 1980 a range of new methods has been added to the traditional approaches of using inactivated or attenuated pathogens as vaccines. Such new methods widen the range of approaches that can be tested, and could lead to many more vaccine candidates being in the development pipeline during the next decade. Most investigators believe that these new methods offer the prospect of vaccines that are freer from adverse reactions. The new methods include:

- conjugation of polysaccharides antigens to proteins, thereby enhancing their immunogenicity;
- protein synthesis using recombinant DNA techniques;
- use of synthetic peptide immunogens;
- attenuation, using genetic engineering;
- use of vaccine vectors, such as attenuated viral and bacterial vaccine strains such as poxviruses, adenovirus, salmonella, or *Bacille Calmette-Guerin* (BCG), that can be genetically engineered to facilitate the presentation of immunogens; and
- immunization with naked DNA.

In addition to these methods that can be used to make vaccine candidates, new or dramatically improved tools in biochemistry and immunology have also emerged in the last decade or so. Such advances include